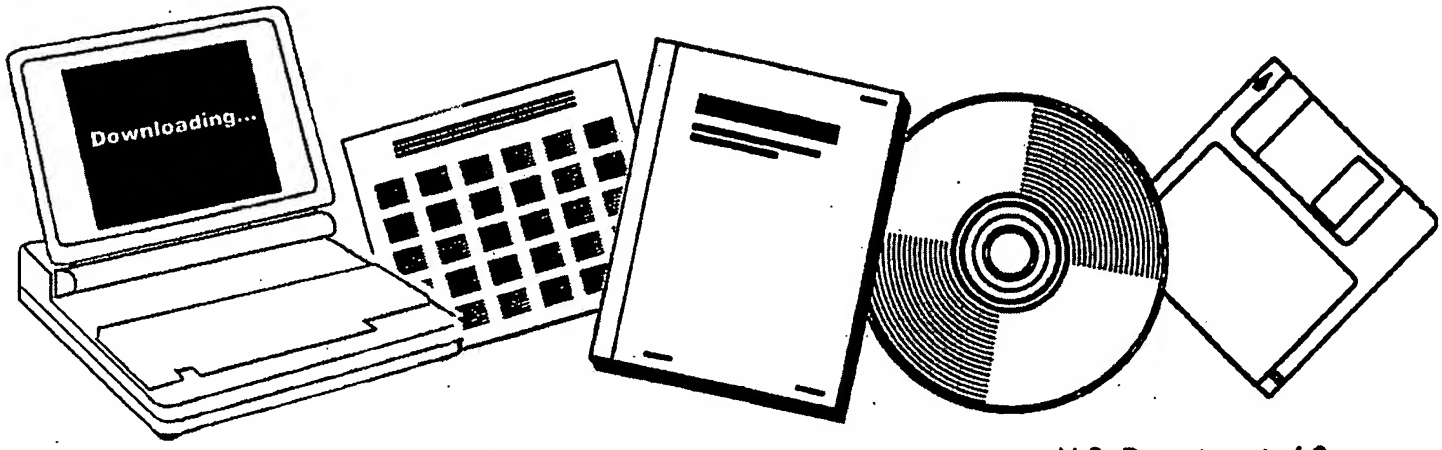
SUPPORT: LETTER FROM DUPONT HASKELL LAB TO USEPA REGARDING RESULTS OF BACTERIAL REVERSE MUTATION ASSAY CONDUCTED WITH 1-PROPENE, 1,1,3,3,3-PENTAFLUORO-, DATED 04/17/00

17 APR



CODING FORMS FOR SRC INDEXING

Microfiche No.		
OTS0573989		
New Doc ID		**Old Doc ID**
88000000077		8EHQ-0100-14638
Date Produced	**Date Received**	**TSCA Section**
01/21/00	01/24/00	8E
Submitting Organization		
E I DUPONT DENEMOURS & CO		
Contractor		
DUPONT HASKEL LABORATORY		
Document Title		
INITIAL SUBMISSION: LETTER FROM DUPONT HASKELL LABS TO USEPA REGARDING RESULTS OF ACUTE INHALATION TOXICITY STUDY IN RATS WITH 1-PROPENE, 1,1,3,3,3-PENTAFLUORO-, DATED 01/21/00		
Chemical Category		
1-PROPENE, 1,1,3,3,3-PENTAFLUORO-		

A 02

INITIAL SUB-MISSION

A-03

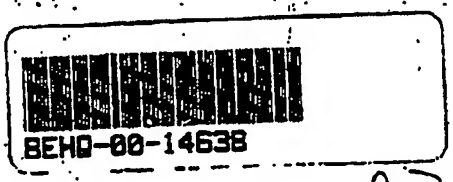
8EHQ-0100-14638

DuPont Haskell Laboratory
for Toxicology and Industrial Medicine
Elkton Road, P.O. Box 50
Newark, DE 19714-0050

RECEIVED
OPPT CBIC

DuPont Haskell Laboratory 2000 JAN 24 PM 12:39

January 21, 2000



Via Federal Express

MR 31691

Document Processing Center (7407)
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U. S. Environmental Protection Agency
401 M Street SW
Washington, DC 20460

Contains NO CBI

RECEIVED
OPPT NCIC
00 FEB 15 AM 11:18

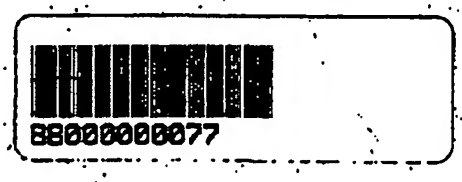
Dear 8(e) Coordinator:

1-Propene, 1,1,3,3,3-pentafluoro-
CAS# 690-27-7

This letter is to inform you of the results of an acute inhalation toxicity study conducted in rats with the above referenced test material.

Four groups of 5 male and 5 female 8-week old Crl:CD®(SD)IGS BR rats were exposed nose-only to gas atmospheres of the test material for a single, 4-hour period. Concentrations tested included 500, 2000, 3300, and 4500 ppm. Rats were observed for clinical signs of toxicity immediately following exposure and during a 14-day recovery period. In addition, approximately 1 day prior to exposure (baseline) and approximately 1 hour and 24 hours after exposure, each rat was systematically observed for functional behavioral anomalies in an open field.

Cage-side examination of rats from the 500 ppm concentration group revealed no clinical signs of toxicity immediately following exposure or during the recovery period. Death and progressively severe clinical signs of toxicity were observed in rats from the remaining groups, and these signs included lethargy, tremors, abnormal posture, prostration, abnormal gait, splayed limbs, and spasms. All clinical signs of toxicity were reversible in surviving rats from all groups.



A-04

For neurobehavioral endpoints in the open field, all rats had scores within normal parameters on the day prior to exposure. Approximately 1 hr after exposure, rats in the 500 ppm group generally appeared to be normal except that 5/10 rats exhibited palpebral closure in the open field. One day after exposure, 2/10 of the 500 ppm rats had low arousal. These signs appeared to be transient and are sometimes identified in control rats in other studies. The lack of a concurrent control group, involving the same confinement characteristics of the nose-only exposure system, precludes a definitive neurobehavioral no-observable-adverse-effect level for this concentration. Signs identified 1 hr after exposure in the 2000 ppm group included abnormal posture, slow righting reflex, poor coordination of movement, abnormal gait, and palpebral closure in the open field. These signs were also present 1 day later, but appeared to be more severe. Mortality occurred 3-5 days after exposure for 6/10 of the rats in the 2000 ppm group. In general, the rats that died exhibited more severe behavioral effects. Some of the rats that survived until the scheduled sacrifice, however, also exhibited some behavioral effects, but to a lesser extent. Both the incidence of mortality (8/10 at 3300 ppm and 9/10 at 4500 ppm) and severity of the behavioral symptoms were greater in the 3300 and 4500 ppm groups than at 2000 ppm.

Under these experimental conditions, the findings described above appear to be reportable, based upon EPA guidance regarding the reportability of such data under TSCA Section 8(e) criteria.

Sincerely,

A. Michael Kaplan

A. Michael Kaplan, Ph.D.
Director - Regulatory Affairs

Contains NO CBI

AMK/JRB:clp
(302)366-5260

05

CERTIFICATE OF AUTHENTICITY

THIS IS TO CERTIFY that the microimages appearing on this microfiche are accurate and complete reproductions of the records of U.S. Environmental Protection Agency documents as delivered in the regular course of business for microfilming.

Date produced 10 (Month) 18 (Day) 00 (Year)

Mary Trulock
Camera Operator

Place Syracuse (City) New York (State)

AMTEK corp

A 01

CODING FORMS FOR SRC INDEXING

Microfiche No.		
OTS0573989		
New Doc ID	Old Doc ID	
89000000142	8EHQ-0200-14638	
Date Produced	Date Received	TSCA Section
02/21/00	02/22/00	8E
Submitting Organization		
E I DUPONT DENEMOURS & CO		
Contractor		
DUPONT HASKELL LAB		
Document Title		
SUPPORT: LETTER FROM DUPONT HASKELL LAB TO USEPA INFORMING OF ADDTNL RESLTS OF ATOX INHALATION & RAT BONE MARROW MICRONUCLEUS ASSAY W/1,1,3,3,3-PENTAFLUOROPROPENE, DATED 02/21/00		
Chemical Category		
1-PROPENE, 1,1,3,3,3-PENTAFLUORO-		

A 02

SUPPORT

A 03

8EHQ-0200-14638

DuPont Haskell Laboratory
for Toxicology and Industrial Medicine
Elkton Road, P.O. Box 50
Newark, DE 19714-0050

RECEIVED
OPPT CBIC

2000 FEB 22 AM 11:45

DuPont Haskell Laboratory

February 21, 2000

Contain NO CBI

Via Federal Express

MR# 32623

Document Processing Center (7407)
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U. S. Environmental Protection Agency
401 M Street SW
Washington, DC 20460

8EHQ-00-14638

Dear 8(e) Coordinator:

1-Propene, 1,1,3,3,3-pentafluoro-
CAS# 690-27-7

This letter is to inform you of additional results from an acute inhalation toxicity study conducted in rats and previously reported to you in our letter of January 21, 2000 and the results of a rat bone marrow micronucleus assay by inhalation.

Acute Inhalation Toxicity Study

Four groups of 5 male and 5 female 8-week old Crl:CD®(SD)IGS BR rats were exposed nose-only to gas atmospheres of the test material for a single, 4-hour period. Concentrations tested included 500, 2000, 3300, and 4500 ppm. Rats underwent a 14-day recovery period following exposure. The lung, liver, and kidneys from rats in the 500 and 2000 ppm groups were examined microscopically. An unexposed control group of rats was not used for comparative purposes.

Compound-related microscopic findings were present in the kidneys of male and female rats exposed to 500 or 2000 ppm of the test compound. In all 2000 ppm rats found dead within 5 days following the exposure, kidney lesions were characterized by severe acute necrosis of renal tubules. Kidney changes in all 500 and 2000 ppm rats that survived the 14-day observation period primarily consisted of regeneration of renal tubules. The extent of tubular regeneration was dose related and tended to be more prominent in male rats compared to females.

Other microscopic findings that may be related to compound exposure include the following:

- Acute necrosis and inflammation in the lungs of 1 female rat exposed to 2000 ppm
- Pulmonary hemorrhage in 2 males exposed to 2000 ppm and 1 female exposed to 500 ppm
- Inflammation and transitional cell hyperplasia of the renal pelvis in 1 female exposed to 2000 ppm
- Periportal fatty change in the liver of 1 male and 1 female exposed to 2000 ppm

In addition to these findings, microscopic changes suggestive of hypertrophy were present in the livers of 500 ppm male rats. However, comparison with a study control group would be necessary to definitively diagnose this change.

RECEIVED
OPPT NCIC
2000 MAR -9 PM 12:11

89000000142

A 04

Rat Bone Marrow Micronucleus Assay by Inhalation

Two groups (low and intermediate concentrations) of 5 male 8-week old Crl:CD®(SD)IGS BR rats and 1 group (high concentration) of 16 male 8-week old Crl:CD®(SD)IGS E.R rats were exposed nose-only to gas atmospheres of the test material for a single, 6-hour period. Concentrations were targeted at 300, 600, and 1200 ppm. A concurrent control group of 10 male rats of the same age was exposed nose-only to air only.

Groups of 5 rats at the 0, 300, and 600 ppm concentrations were sacrificed 24 hours post exposure and evaluated for micronucleated polychromatic erythrocytes (MNPCEs). The first 10 of 16 animals from the 1200 ppm group were also sampled 24 hours (5 rats) and 48 hours (5 rats) after treatment and evaluated for micronuclei. The remaining 6 rats from this group were sacrificed without evaluation. In addition, a group of 5 vehicle control rats was sacrificed 48 hours post exposure and evaluated for MNPCEs.

A statistically significant increase in the frequency of MNPCEs was observed in rats exposed to 1200 ppm and sampled 24 hours after treatment. Rats at the highest concentration that were sampled 48 hours post exposure did not show a statistically significant elevation in MNPCE scores; however, 2 out of 5 rats did respond comparably to positive control rats.

The MNPCE counts for the 2 lower concentrations were not significantly elevated over the vehicle controls; however 2 out of 5 animals in each group did respond comparably to positive control rats. In addition, the Jonckheere test for trends from the 0 to the 1200 ppm groups was statistically significant at a level of alpha = 0.05.

Under these experimental conditions, the findings described above appear to be reportable, based upon EPA guidance regarding the reportability of such data under TSCA Section 8(e) criteria.

Sincerely,

A. Michael Kaplan, Ph.D.
Director - Regulatory Affairs

AMK/JRB:clp
(302)366-5260

5

CERTIFICATE OF AUTHENTICITY

THIS IS TO CERTIFY that the microimages appearing on this microfiche are accurate and complete reproductions of the records of U.S. Environmental Protection Agency documents as delivered in the regular course of business for microfilming.

Date produced 10 (Month) 18 (Day) 00 (Year) Mary Trubeck Camera Operator

Place Syracuse (City) New York (State)

AMTEK corp

A 01

CODING FORMS FOR SRC INDEXING

Microfiche No.		
OTS0573989		
New Doc ID		Old Doc ID
89000000186		8EHQ-0400-14638
Date Produced	Date Received	TSCA Section
04/17/00	04/18/00	8E
Submitting Organization		
E I DUPONT DENEMOURS & CO		
Contractor		
DUPONT HASKELL LAB		
Document Title		
SUPPORT: LETTER FROM DUPONT HASKELL LAB TO USEPA REGARDING RESULTS OF BACTERIAL REVERSE MUTATION ASSAY CONDUCTED WITH 1-PROPENE, 1,1,3,3,3-PENTAFLUORO-, DATED 04/17/00		
Chemical Category		
1-PROPENE, 1,1,3,3,3-PENTAFLUORO-		

A 02

SUPPORT

A 03

8EHQ-0400-14638

DuPont Haskell Laboratory
for Toxicology and Industrial Medicine
Elkton Road, P.O. Box 50
Newark, DE 19714-0050

DuPont Haskell Laboratory

April 17, 2000

MR 34847

Via Federal Express

Document Processing Center (7407)
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U. S. Environmental Protection Agency
401 M Street SW
Washington, DC 20460-0001

Contain NO CBI

Dear 8(e) Coordinator:

1-Propene, 1,1,3,3,3-pentafluoro-
8EHQ-00-14638

This letter is to inform you of the results of a bacterial reverse mutation assay conducted with the above referenced test substance.

The test substance was evaluated in the bacterial reverse mutation assay using *Salmonella typhimurium* strains TA97a, TA98, TA100, TA1535, and *Escherichia coli* strain WP2 *uvrA* (pKM101) in the presence and absence of an exogenous metabolic activation system (Aroclor ®-induced rat liver S9).

Tester strains were exposed to the test substance at actual mean concentrations of approximately 0.08, 0.14, 0.5, 1.1 and 4.8% in the presence and absence of S9. Preliminary testing at concentrations of 15% or greater were cytotoxic to bacteria. Test substance-related toxicity, as evidenced by the reduction of the microcolony background lawn and/or as a concentration-related reduction in the mean number of revertants per plate, was observed with *S. typhimurium* strain TA97a in the presence and absence of the metabolic activation system at 1.1 and 4.8%. Evidence of mutagenicity was detected with tester strain TA98 without activation at 0.5% or greater, and with TA1535 with activation at 4.8%. Both strains exhibited concentration-related increases of the mean revertants per plate compared to their concurrent negative controls. Under the conditions of this study, the test substance was concluded to be positive for the induction of mutagenicity in the bacterial reverse mutation test.

A 04

Under these experimental conditions and when viewed in light of the positive results of an *in vivo* micronucleus assay previously reported to the agency (2/21/00), the findings described above appear to be reportable based upon EPA guidance regarding the reportability of such data under TSCA Section 8(e) criteria.

Sincerely,

A. Michael Kaplan, Ph.D.
Director - Regulatory Affairs

AMK/RV:clp
(302) 366-5260

A 05

CERTIFICATE OF AUTHENTICITY

THIS IS TO CERTIFY that the microimages appearing on this microfiche are accurate and complete reproductions of the records of U.S. Environmental Protection Agency documents as delivered in the regular course of business for microfilming.

Date produced 10 (Month) 18 (Day) 00 (Year) Mary Furbeck Camera Operator

Place Syracuse (City) New York (State)

AMTEK corp